Set	Items	Description
S1	166	AU="GJERSET R" OR AU="GJERSET R A" OR AU="GJERSET R A; SMITH L; BARTHOLOMEW R M; BOGGIAN" OR AU="GJERSET R." OR AU="GJERSET R.A." OR AU="GJERSET RA" OR AU="GJERSET RUTH" OR AU="GJERSET RUTH A" OR AU="GJERSET-PARTRIDGE R A"
S2	117	S1 NOT PY>1996
S3	42	RD (unique items)
S4	158744	P53
S5	6110	P(W)53
S6	164008	S4 OR S5
S7	5224525	CANCER OR TUMOR OR TUMOUR OR CARCINOMA OR GLIOBLASTOMA
S8	1414102	BLASTOMA OR NEUROBLASTOMA OR LEUKEMIA OR LYMPHOMA OR SARCOMA
S9	6022162	S7 OR S8
S10	130245	S6 AND S9
S11	150021	ADENOVIR?
S12	10378	EXPRESSION(W)CONSTRUCT? ?
S13	134280	GENE(W)THERAPY
S14	141570	S12 OR S13
S15	6993	S10 AND S14
S16	4048	S15 AND S11
S17	51	AU="GJERSET R"
S18	134831	E(W)1
S19	126571	"E1"
S20	253762	S18 OR S19
S21	746	S16 AND S20
S22	149355	CYTOMEGALOVIRUS OR CMV
S23	626848	PROMOTER
S24	77	S21 NOT PY>1996
S25	64	RD (unique items)
S26	21184	S22(S)S23
S27	30	S25 AND S26
S28	34	S25 NOT S27
S29	42703	C(W)JUN
S30	77346	C(W)FOS
S31	0	POLY(W)ADP(W)RIBOSE(W)POLYNERASE
S32	5272	DNA(W)POLYMERASE(W)BETA
S33	19599	TOPOISOMERASE(W)I
S34	0	D(W)MP(W)SYNTHASE
S35	26	HMTII(W)A
S36	3592	URACIL(W)DNA(W)GLYCOSYLASE
S37	30	ALKYL(W)N(W)PURINE(W)DNA(W)GLYCOSYLASE
S38	743	DNA(W)LIGASE(W)(III OR IV)
S39	291	HAP(W)1
S40	7072	REF(W)1
S41	13571	POLY(W)ADP(W)RIBOSE(W)POLYMERASE
S42	492871	PROTEIN(W)KINASE
S43	6601289	S29 OR 30 OR S32 OR S33 OR S34 OR S35 OR S36 OR S37 OR S38 OR S39 OR S40 OR S41
S44	647	S21 AND S43
S45	45	S44 NOT PY>1996
S46	43	RD (unique items)
S47	43721	RETINOID
S48	4	SR11220
S49	2	SR(W)11220
S50	4799	3(W)AMINOBENZAMIDE
S51	0	S46 AND S47
S52	0	S46 NOT (S25 OR S27 OR S28)
S53	61	S15 AND S47
S54	5	S53 NOT PY>1996
S55	5	RD (unique items)

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S56      13583   S9 AND S47
S57          6   S48 OR S49
S58          3   S50 AND S47 AND S9
S59          3   S50 AND S47
S60      13583   S9 AND S47
S61       1306   S9 AND S50
S62     149675   CISPLATIN
S63      33098   CARBOPLATIN
S64      10116   VP16
S65       8923   TENIPOSIDE
S66      34491   DAUNORUBICIN
S67     135778   DOXORUBICIN
S68      35805   DACTINOMYCIN
S69      76092   MITOMYCIN
S70       1515   PLICAMYCIN
S71      73404   BLEOMYCIN
S72      18945   PROCARBAZINE
S73      31630   NITROSOUREA
S74     190938   CYCLOPHOSPHAMIDE
S75         67   BISULFAN
S76      32698   MELPHALAN
S77      21033   CHLORAMBUCIL
S78      23016   IFOSFAMIDE
S79          4   MERCHLOREHTAMINE
S80      36326   TAXOL
S81          2   TASOTERE
S82      50389   ANTHRACYCLINE? ?
S83    2933465   RADIATION
S84    3530257   S62 OR S63 OR S64 OR S65 OR S66 OR S67 OR S68 OR S69 OR S70
                 OR S71 OR S72 OR S73 OR S74 OR S75 OR S76 OR S78 OR S79 OR S-
                 80 OR S81 OR S82 OR S83
S85       1289   S60 AND S84
S86        532   S61 AND S84
S87          2   S85 AND S86
S88       1819   S85 OR S86
S89        839   S88 NOT PY>1995
S90        615   RD (unique items)
S91    2374197   INJECTED OR INJECTION
S92         91   S90 AND S91
S93     572330   PERFUSION OR PERFUSED
S94          8   S92 AND S93
?
```

3/3,AB/1 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08459461 96116684
Use of wild-type p53 to achieve complete treatment sensitization of tumor cells expressing endogenous mutant p53.
Gjerset RA ; Turla ST; Sobol RE; Scalise JJ; Mercola D; Collins H; Hopkins PJ
Sidney Kimmel Cancer Center, San Diego, California 92121, USA.
Molecular carcinogenesis (UNITED STATES) Dec 1995, 14 (4) p275-85, ISSN 0899-1987 Journal Code: AEQ
Contract/Grant No.: RO1 CA63783, CA, NCI
Languages: ENGLISH
Document type: JOURNAL ARTICLE
It is known that transfer of the wild-type p53 gene into p53-negative cells from transgenic mice increases their sensitivity to drug and radiation-induced apoptosis. However, unlike many human tumors, these transgenic cells do not express mutant p53, and it is not known from these earlier studies whether wild-type p53 dominates the effects of mutant p53 with respect to drug and radiation sensitivity. We addressed this question in glioblastoma, a disease characterized by an unusually high level of intrinsic resistance to therapy and poor prognosis: mean survival time from diagnosis is only about 1 yr. We introduced the gene for wild-type p53 into human T98G glioblastoma cells, which express endogenous mutant p53 but not wild-type p53. Stable transfectants that co-expressed mutant and wild-type p53 had enhanced sensitivity to cisplatin and gamma radiation, compared with parental cells, control vector-transduced cells, and transduced cells that had lost expression of wild-type p53. Transient wild-type p53 expression after high-efficiency gene transfer by a p53 adenovirus also sensitized the cells to cisplatin and correlated with the induction of apoptosis. The sensitization effect was also observed in p53 adenovirus-infected H23 small cell lung carcinoma cells, which express endogenous mutant p53. Therefore, wild-type p53 gene transfer has dominant effects over mutant p53 in sensitizing tumor cells to therapy, which supports the potential of p53 gene therapy to enhance the efficacy of traditional therapy.

3/3,AB/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08425019 96020486
Comparison of gene therapy with interleukin-2 gene modified fibroblasts and tumor cells in the murine CT-26 model of colorectal carcinoma.
Shawler DL; Dorigo O; **Gjerset RA** ; Royston I; Sobol RE; Fakhrai H
Sidney Kimmel Cancer Center, San Diego, CA 92121, USA.
Journal of immunotherapy with emphasis on tumor immunology (UNITED STATES) May 1995, 17 (4) p201-8, ISSN 1067-5582 Journal Code: BZH
Contract/Grant No.: AG0353-06, AG, NIA
Languages: ENGLISH
Document type: JOURNAL ARTICLE
We compared the efficacy of gene therapy mediated by interleukin-2 (IL-2) gene-modified tumor cells to gene therapy mediated by IL-2 transduced fibroblasts in the CT-26 model of murine colorectal carcinoma. We transduced CT-26 tumor cells and BALB/c 3T3 fibroblasts with three different retroviral vectors using three different promoters for the human IL-2 gene: DC/TKIL-2 (thymidine kinase promoter), LXSN-iIL2 (long terminal repeat promoter), and LNCX-iIL2 (cytomegalovirus promoter). These

transductions resulted in CT-26 and 3T3 subclones that secreted different amounts of IL-2. Immunization of animals with either CT-26/IL-2 cells or with fibroblast/IL-2 cells mixed with CT-26 induced similar levels of immunity that protected 62-82% of animals against a subsequent tumor challenge with parental CT-26. However, mice developed tumors at the site of inoculation in 46% of the animals immunized with CT-26/IL-2 cells. In a separate experiment, CT-26/IL-2 cells were exposed to 6,000 cGy of gamma irradiation to prevent tumor growth at the site of inoculation. Although the CT-26/IL-2 cells continued to secrete IL-2 after irradiation, they were no longer effective at inducing antitumor immunity. In contrast, both irradiated and nonirradiated fibroblast/IL-2 cells, mixed with irradiated CT-26, were equally effective at inducing antitumor immunity. These data suggest that in the CT-26 model, fibroblast-mediated IL-2 gene therapy has advantages for the induction of antitumor immunity and abrogation of tumorigenic potential at the site of inoculation compared with tumor cell-mediated IL-2 gene therapy.

3/3,AB/7 (Item 7 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07628528 93232299
Expression of SV40 virus large T antigen by recombinant adenoviruses activates proliferation of corneal endothelium in vitro.
Feldman ST; **Gjerset R** ; Gately D; Chien KR; Feramisco JR
Department of Ophthalmology, University of California, San Diego, La Jolla 92093.
Journal of clinical investigation (UNITED STATES) Apr 1993, 91 (4) p1713-20, ISSN 0021-9738 Journal Code: HS7
Contract/Grant No.: AG000353, AG, NIA
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Infection with the Ad5-SVR4 virus was used to introduce the large T antigen encoding region of the SV40 virus into bovine and human corneal endothelial cells. Expression of large T antigen occurred in 40% of bovine corneal endothelial cells after a 24-h incubation time versus 12% after 8 h of incubation. By 48 h after infection, almost all (92.8%) bovine corneal endothelial cells expressed large T antigen. Bovine and human corneal endothelial cells which expressed large T antigen proliferated and the characteristic morphologic features of corneal endothelium were maintained. This method may enable growth of enough corneal endothelium to perform studies to elucidate the biochemical mechanisms involved in regulating endothelial cell function.

3/3,AB/8 (Item 8 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07541979 93253056
P53 mutation in acute T cell lymphoblastic leukemia is of somatic origin and is stable during establishment of T cell acute lymphoblastic leukemia cell lines.
Yeargin J; Cheng J; Yu AL; **Gjerset R** ; Bogart M; Haas M
University of California San Diego Cancer Center, Department of Pathology, La Jolla 92093-0063.
Journal of clinical investigation (UNITED STATES) May 1993, 91 (5) p2111-7, ISSN 0021-9738 Journal Code: HS7
Contract/Grant No.: R01CA56075, CA, NCI; U10CA28439, CA, NCI
Languages: ENGLISH

Document type: JOURNAL ARTICLE
Samples donated by patients with T cell acute lymphoblastic leukemia (T-ALL) were screened for mutations of the p53 tumor suppressor gene. Peripheral blood cells of T-ALL relapse patient H.A. were found to possess a heterozygous point mutation at codon 175 of the p53 gene. To determine whether this was an inherited mutation, a B cell line (HABL) was established. Leukemic T cell lines (HATL) were concurrently established by growing peripheral blood leukemic T cells at low oxygen tension in medium supplemented with IGF-I. Previously we had shown that > 60% of leukemic T cell lines possessed mutations in the p53 gene (Cheng, J., and M. Hass. 1990. Mol. Cell. Biol. 10:5502), mutations that might have originated with the donor's leukemic cells, or might have been induced during establishment of the cell lines. To answer whether establishment of the HATL lines was associated with the induction of p53 mutations, cDNAs of the HATL and HABL lines were sequenced. The HATL lines retained the same heterozygous p53 mutation that was present in the patient's leukemic cells. The HABL line lacked p53 mutations. Immunoprecipitation with specific anti-p53 antibodies showed that HATL cells produced p53 proteins of mutant and wild type immunophenotype, while the HABL line synthesized only wild-type p53 protein. The HATL cells had an abnormal karyotype, while the HABL cells possessed a normal diploid karyotype. These experiments suggest that (a) p53 mutation occurred in the leukemic cells of relapse T-ALL patient HA; (b) the mutation was of somatic rather than hereditary origin; (c) the mutation was leukemia associated; and (d) establishment of human leukemia cell lines needs not be associated with in vitro induction of p53 mutations. It may be significant that patient HA belonged to a category of relapse T-ALL patients in whom a second remission could not be induced.

3/3,AB/23 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

10782536 BIOSIS NO.: 199799403681
Enhancement of antitumor effects of p53 gene therapy by combination with DNA-damaging agents.
AUTHOR: Harper M E(a); Cristiano R; Spitz F; Nguyen D; **Gjerset R A** ; Roth J A
AUTHOR ADDRESS: (a)Introgen Therapeutics Inc., Houston, TX**USA
JOURNAL: Cancer Gene Therapy 3 (6 CONF. SUPPL.):pS41-S42 1996
CONFERENCE/MEETING: Fifth International Conference on Gene Therapy of Cancer San Diego, California, USA November 14-16, 1996
ISSN: 0929-1903
RECORD TYPE: Citation
LANGUAGE: English
1996

3/3,AB/26 (Item 5 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

09710204 BIOSIS NO.: 199598165122
Dominant effect of transduced wild-type p53 over endogenous mutant p53 in sensitizing tumor cells to therapy.
AUTHOR: **Gjerset R A** ; Turla S T; Scalise J J; Sobol R E; Shawler D L; Hopkins P J
AUTHOR ADDRESS: San Diego Reg. Cancer Cent., 3099 Science Park Road, San Diego, CA 92121**USA
JOURNAL: Proceedings of the American Association for Cancer Research Annual Meeting 36 (0):p21 1995

Set	Items	Description
S1	175383	P53
S2	5556993	CANCER OR CARCINOMA OR NEOPLAS? OR SARCOMA OR MELANOMA OR GLIOBLASTOMA OR LEUKEMIA
S3	121250	S1 AND S2
S4	366133	APOPTOSIS
S5	176209	S ANTISENSE OR CISPLATIN OR CARBOPLATIN
S6	207730	VP16 OR TENIPOSIDE OR DAUNORUBICIN OR DOXORUBICIN OR DACTINOMYCIN
S7	160193	MITOMYCIN OR PLICAMYCIN OR BLEOMYCIN OR PROCARBAZINE
S8	228596	NITROSOUREA OR CYCLOPHOSPHAMIDE OR BISULFAN
S9	74404	MELPHALAN OR CHLORAMBUCIL OR IFOSFAMIDE OR MERCHLOREHTAMINE
S10	3134843	TAXOL OR TAXOTERE OR ANTHRACYCLINE? ? OR RADIATION
S11	149093	ADENOVIRUS OR ADENOVIRAL
S12	0	E1
S13	5760	REPLICATION(W)DEFICIENT
S14	1251	(CYTOMEGALOVIRUS OR CMV)(S)PROMOTOR
S15	25264	S3 AND S4
S16	133873	"E1"
S17	5927	S11 AND S16
S18	473	S17 AND S13
S19	53	S15 AND S18
S20	46	RD (unique items)
S21	6647	S15 AND (S6 OR S7 OR S8 OR S9 OR S10)
S22	34	S20 AND S21
S23	0	S22 NOT PY>1996
S24	0	S20 NOT PY>1996
S25	0	S11 AND S12
S26	5927	S11 AND S16
S27	753	S1 AND S26
S28	619	S27 AND S2
S29	235	S28 AND (S6 OR S7 OR S8 OR S9 OR S10)
S30	7	S29 NOT PY>1996

?

CONFERENCE/MEETING: Eighty-sixth Annual Meeting of the American Association for Cancer Research Toronto, Ontario, Canada March 18-22, 1995
ISSN: 0197-016X
RECORD TYPE: Citation
LANGUAGE: English
1995

3/3,AB/41 (Item 1 from file: 357)
DIALOG(R)File 357:Derwent Biotechnology Abs

0174147 DBA Accession No.: 95-00968
Enhancement of tumor sensitivity to chemotherapy and radiation by wild-type p53 gene transfer- tumor suppressor gene transfer for increased cytostatic and gamma-irradiation sensitivity for e.g. glioblastoma gene therapy (conference abstract)
AUTHOR: **Gjerset R A** ; Turla S; Scalise J; Sobol R; Shawler D; Isabella P
CORPORATE AFFILIATE: San-Diego-Reg.Cancer-Cent.
CORPORATE SOURCE: San Diego Regional Cancer Center, 3099 Science Park Road, San Diego, CA 92121, USA.
JOURNAL: Cancer Gene Ther. (1, 4, 330) 1994
CODEN: 2815V
CONFERENCE PROCEEDINGS: Gene Therapy of Cancer, 3rd International Conference, San Diego, CA, 10-12 November, 1994.
LANGUAGE: English
ABSTRACT: The effect of introduction of wild-type p53 into glioblastoma cells expressing endogenous mutant p53 on sensitivity to chemotherapeutic drugs and radiation was investigated. Following wild-type p53 gene transfer, stable transfectants were selected and characterized. Cells co-expressing mutant and wild-type p53 had markedly enhanced sensitivity to cisplatin and gamma-irradiation. A certain cisplatin or radiation doses, viability of wild-type p53-expressing cells was virtually abolished. This suggests that p53 gene therapy could be a useful adjuvant to traditional chemotherapy and radiation, by re-establishing apoptosis pathways, particularly in therapy of glioblastoma multiforme (the most malignant form of astrocytoma), which is relatively radiation resistant and responds poorly to most chemotherapeutic drugs. Since p53 deletions or mutations may be involved in up to half of glioblastomas, p53 gene therapy even under conditions providing only transient expression could provide a means to enhance or restore treatment sensitivity to a substantial proportion of these tumors. (0 ref)

3/3,AB/42 (Item 1 from file: 349)
DIALOG(R)File 349:PCT Fulltext

00399019
ENHANCING THE SENSITIVITY OF TUMOR CELLS TO THERAPIES
AMELIORATION DE LA SENSIBILITE DE CELLULES TUMORALES A DES THERAPIES
Patent Applicant/Assignee:
SAN DIEGO REGIONAL CANCER CENTER
Inventor(s):
GJERSET Ruth A
SOBOL Robert E
Patent and Priority Information (Country, Number, Date):
Patent: WO 9530002 A2-A3 19951109
Application: WO 95US5272 19950428 (PCT/WO US9505272)

Priority Application: US 94236221 19940429; US 94248814 19940524; US 94335461 19941107
Designated States: AU CA JP KR AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE
Publication Language: English
Fulltext Word Count: 11680

English Abstract
A method for enhancing the effect of a cancer therapy by introducing wild-type therapy sensitizing gene activity into tumor cells having mutant therapy sensitizing gene activity and subjecting the tumor cells to a cancer therapy such as chemotherapy, radiotherapy, biological therapy including immunotherapy, cryotherapy and hyperthermia.

French Abstract
L'invention concerne un procede d'amelioration de l'effet d'une therapie du cancer consistant a introduire une activite genique de type sauvage de sensibilisation a une therapie dans des cellules tumorales presentant une activite genique mutante de sensibilisation a une therapie, et a soumettre les cellules tumorales a une therapie du cancer telle qu'une chimiotherapie, une radiotherapie, une therapie biologique, y compris une immunotherapie, une cryotherapie et une hyperthermie.
?

27/3,AB/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08154790 95346687
High-efficiency gene transfer and high-level expression of wild-type p53 **in human lung** cancer **cells mediated by recombinant** adenovirus.
Zhang WW; Fang X; Mazur W; French BA; Georges RN; Roth JA
Department of Thoracic and Cardiovascular Surgery, University of Texas M.D. Anderson Cancer Center, Houston 77030, USA.
Cancer gene therapy (UNITED STATES) Mar 1994, 1 (1) p5-13, ISSN 0929-1903 Journal Code: CE3
Contract/Grant No.: CA 16672, CA, NCI; RO1 CA 45187, CA, NCI
Languages: ENGLISH
Document type: JOURNAL ARTICLE
A replication-defective and helper-independent recombinant **p53 adenovirus** was generated. The virus, Ad5CMV-**p53** , carries an expression cassette that contains human **cytomegalovirus E1 promoter** , human wild-type **p53** cDNA, and SV40 early polyadenylation signal. Four human non-small-cell lung **cancer** cell lines representing differences in **p53** configuration were used to evaluate the Ad5CMV-**p53** virus. In the H358 cell line, which has a homozygous deletion of **p53** , the **p53** gene was transferred with 97% to 100% efficiency, as detected by immunohistochemical analysis, when the cells were infected with Ad5CMV-**p53** at a multiplicity of infection of 30 to 50 plaque-forming units/cell. Western blots showed that the **p53** protein was expressed at a high level. The protein expression peaked at day 3 after infection and lasted for at least 15 days. Growth of the Ad5CMV- **p53** virus-infected H358 cells was inhibited 79%, whereas that of noninfected cells or the cells infected with the control virus was not inhibited. Growth of cell line H322, which has a point mutation in **p53** , was inhibited 72% by Ad5CMV-**p53** , while that of cell line H460 containing wild-type **p53** was less affected (28% inhibition). Tests in nude mice demonstrated that tumorigenicity of the Ad5CMV-**p53** -treated H358 cells was greatly inhibited. In a mouse model of orthotopic human lung **cancer** , the tumorigenic H226Br cells, with a point mutation in **p53** , were inoculated intratracheally 3 days before the virus treatment. Intratracheal instillation of Ad5CMV- **p53** prevented **tumor** formation.(ABSTRACT TRUNCATED AT 250 WORDS)

27/3,AB/3 (Item 1 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

04632414 Genuine Article#: TY216 Number of References: 31
Title: GROWTH-INHIBITION OF HUMAN CERVICAL- CANCER **CELLS WITH THE RECOMBINANT** ADENOVIRUS P53 **IN-VITRO** (Abstract Available)
Author(s): HAMADA K; ZHANG WW; ALEMANY R; WOLF J; ROTH JA; MITCHELL MF
Corporate Source: UNIV TEXAS,MD ANDERSON CANCER CTR,DEPT THORAC &CARDIOVASC SURG,SECT THORAC MOLEC ONCOL/HOUSTON//TX/77030; UNIV TEXAS,MD ANDERSON CANCER CTR,DEPT GYNECOL ONCOL/HOUSTON//TX/77030
Journal: GYNECOLOGIC ONCOLOGY, 1996, V60, N3 (MAR), P373-379
ISSN: 0090-8258
Language: ENGLISH Document Type: ARTICLE
Abstract: Human papillomavirus (HPV) has been identified in the majority of invasive cancers of the uterine cervix sampled and has been found to contribute in a significant way to the genesis of human cervical **cancer** . HPV has two transforming genes that encode the oncoproteins E6 and E7, E6 can form complexes with **p53** and promote **p53** degradation. We introduced wild-type **p53** into a cervical **cancer** cell line via a recombinant **adenoviral** vector, Ad5CMV-**p53** . Human cervical **cancer**

cell line HeLa, which has HPV type 18 and wild-type **p53** , was used in this study. Cells were grown in RPMI medium supplemented with 10% heat-inactivated fetal bovine serum, Ad5CMV-**p53** was created by inserting the **cytomegalovirus promoter** , wild-type **p53** cDNA, and SV40 polyadenylation signal in a minigene cassette into the **E1** -deleted region of the modified Ad5 **adenovirus** . The transduction efficiency was 100% when a dose ensuring a multiplicity of infection of 100 or greater was used, The **p53** protein was detected in Ad5CMV-**p53** -infected cells by immunohistochemical and Western blot analyses. The growth of the Ad5CMV-**p53** -infected cells was greatly suppressed as detected by both cell count and [H-3]thymidine incorporation assay. These data suggest that transfection of HPV-positive cervical **cancer** cells with a wild-type **p53** gene in a form such as Ad5CMV-**p53** is a potential novel therapy for cervical **cancer** . (C) 1996 Academic Press, Inc.

27/3,AB/4 (Item 1 from file: 73)
DIALOG(R)File 73:EMBASE

06245533 EMBASE No: 1995282364
Department of Health and Human Services, National Institutes of Health, Recombinant DNA Advisory Committee. Minutes of Meeting, December 1-2, 1994
Brinckerhoff C.E.; Capron A.M.; Chase G.A.; DeLeon P.A.; Doi R.H.; Erickson R.P.; Glorioso J.C.; Haselkorn R.; Meyers A.S.; Miller A.D.; Motulsky A.G.; Parkman R.; Ross G.S.; Saha B.K.; Samulski R.J.; Secundy M.G.; Smith B.R.; Straus S.E.; Walters L.B.; et al.
Dept. of Medicine, Dartmouth Medical School, 2 Maynard Street,Hanover, NH 03755 United States
Human Gene Therapy (HUM. GENE THER.) (United States) 1995, 6/8 (1065-1124)
CODEN: HGTHE ISSN: 1043-0342
DOCUMENT TYPE: Journal; Conference Paper
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

Drs. Alan P. Venook and Robert S. Warren of the University of California at San Francisco, San Francisco, California, may conduct gene transfer experiments on 27 subjects (>= 18 and <= 75 years of age) with hepatocellular **carcinoma** or liver metastasis of colorectal **cancer** . The **adenovirus** vector, ACN53, to transduce the human **p53** **tumor** suppressor gene is derived from **adenovirus** type 5 by replacing the **E1** region including E1a, E1b, and protein IX coding region with a **p53** expression cassette driven by the **CMV** **promoter** . The vector is additionally deleted for 1.9 kb DNA sequences in the E3 region. ACN53 will be administered as a single bolus infusion via a hepatic artery catheter. This Phase I dose-escalation trial is designed primarily to assess the safety of ACN53 and secondarily its biological efficacy. Biological efficacy including efficiency and stability of gene transfer will be studied by analysis of **tumor** tissues obtained 7 days following gene transfer. Clinical evidence of anti-**tumor** efficacy will also be collected. The effect of ACN53 dosage on patient tolerance and toxicity will be evaluated in the dose escalation cohorts. As an important part of this objective, the pharmacokinetics of ACN53 will be studied.

27/3,AB/5 (Item 1 from file: 98)
DIALOG(R)File 98:General Sci Abs/Full-Text

03051107 H.W. WILSON RECORD NUMBER: BGSI95051107

Viral vectors in gene therapy.
Smith, Alan E
Annual Review of Microbiology (Annu Rev Microbiol) v. 49 ('95) p. 807-38
DOCUMENT TYPE: Feature Article
SPECIAL FEATURES: bibl il ISSN: 0066-4227
LANGUAGE: English
COUNTRY OF PUBLICATION: United States
WORD COUNT: 14692

ABSTRACT: The use of DNA as a drug is both appealing and simple in concept. Indeed in many instances the feasibility of such an approach has been established using model systems. In practical terms, however, the delivery of DNA to human tissues presents a wide variety of problems that differ with each potential therapeutic application. In this review, the design, production, and application of viral vectors for human **gene therapy** are considered. Although viral vectors are an obvious starting point because viruses have evolved efficient mechanisms to introduce and express their nucleic acid into recipient cells, by the same token the viral hosts have evolved sophisticated mechanisms to rid themselves of such pathogens. The challenge for the therapeutic use of viral vectors is to achieve efficient and often extended expression of the exogenous gene while evading the host defenses. Methodology used and progress towards that goal are reviewed. Reprinted by permission of the publisher.

27/3,AB/6 (Item 1 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00785712
Recombinant DNA virus and method for preparation thereof
Rekombinanter DNA Virus und Methoden seiner Herstellung
Virus ADN recombinant et sa preparation
PATENT ASSIGNEE:
SUMITOMO PHARMACEUTICALS COMPANY, LIMITED, (653536), 2-8, Dosho-machi 2-chome, Chuo-ku, Osaka-shi, Osaka-fu 541, (JP), (applicant designated states: AT;BE;CH;DE;DK;ES;FI;FR;GB;GR;IE;IT;LI;NL;PT;SE)
INVENTOR:
Saito, Izumi, 37-15-412, Yoyogi-2-chome, Shibuya-ku, Tokyo, (JP)
Kanegae, Yumi, 10-14-1405, Nishigotanda-8-chome, Shinagawa-ku, Tokyo, (JP)
Nakai, Michio, 3-41-309, Denpo-5-chome, Konohana-ku, Osaka-shi, (JP)
LEGAL REPRESENTATIVE:
Kolb, Helga, Dr. Dipl.-Chem. (49372), Hoffmann Eitle, Patent- und Rechtsanwalte, Arabellastrasse 4, 81925 Munchen, (DE)
PATENT (CC, No, Kind, Date): EP 732405 A1 960918 (Basic)
APPLICATION (CC, No, Date): EP 96301766 960314;
PRIORITY (CC, No, Date): JP 9584891 950315; JP 95276335 950929
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI; NL; PT; SE
INTERNATIONAL PATENT CLASS: C12N-015/86; C12N-007/01;

ABSTRACT EP 732405 A1
A recombinant DNA virus for transfecting an animal cell and bearing a foreign gene and a promoter capable of regulating expression of the foreign gene is completely deleted of the function of E2A gene. The recombinant DNA virus can thus stably transduce the foreign gene into various animal cells, which leads to continuous expression of the foreign gene in the animal cells. The continuous expression of the foreign gene can provide an effective treatment of hereditary disease.

ABSTRACT WORD COUNT: 93

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	EPAB96	1133
SPEC A	(English)	EPAB96	17958
Total word count - document A			19091
Total word count - document B			0
Total word count - documents A + B			19091

27/3,AB/10 (Item 4 from file: 349)
DIALOG(R)File 349:PCT Fulltext

00435289
ADENOVIRUS **VECTORS FOR** GENE THERAPY
VECTEURS D' ADENOVIRUS **POUR THERAPIE GENIQUE**
Patent Applicant/Assignee:
GENZYME CORPORATION
Inventor(s):
ARMENTANO Donna
ROMANCZUK Helen
WADSWORTH Samuel C
Patent and Priority Information (Country, Number, Date):
Patent: WO 9630534 A1 19961003
Application: WO 96US3818 19960320 (PCT/WO US9603818)
Priority Application: US 95409874 19950324; US 95540077 19951006
Designated States: AL AM AT AU AZ BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU IS JP KE KR KZ LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI TM TR TT UA UG UZ VN KE LS MW SD SZ UG AM AZ BY KG KZ MD RU TJ TM AT BE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN ML MR NE TG
Publication Language: English
Fulltext Word Count: 10634
English Abstract
The present invention relates to novel **adenovirus** vectors for use in **gene therapy** which are designed to prevent the generation of replication-competent **adenovirus** (RCA) during in vitro propagation and clinical use. The invention also provides methods for the production of the novel virus vectors. These vectors maximize safety for clinical applications in which **adenovirus** vectors are used to transfer genes into recipient cells for **gene therapy** .

French Abstract
La presente invention se rapporte a de nouveaux vecteurs d'**adenovirus** qui sont utilises dans la therapie genique et qui sont concus pour empecher la generation d'**adenovirus** capables de se repliquer (RCA) pendant la propagation in vitro et l'utilisation clinique. L'invention decrit egalement des methodes de production de nouveaux vecteurs de virus. Ces vecteurs maximisent la securite concernant les applications cliniques dans lesquelles les vecteurs d'**adenovirus** sont utilises pour transferer des genes dans des cellules receveuses pour la therapie genique.

27/3,AB/11 (Item 5 from file: 349)
DIALOG(R)File 349:PCT Fulltext

00429581

METHODS OF PREPARATION AND USE OF RECOMBINANT ADENOVIRAL **VECTORS**

PROCEDES DE PREPARATION ET D'UTILISATION DE VECTEURS ADENOVIRAUX **RECOMBINES**

Patent Applicant/Assignee:
THE GOVERNMENT OF THE UNITED STATES OF AMERICA represented by THE
SETH Prem K
COWAN Kenneth
Inventor(s):
SETH Prem K
COWAN Kenneth

Patent and Priority Information (Country, Number, Date):
Patent: WO 9625507 A2-A3 19960822
Application: WO 96US2336 19960216 (PCT/WO US9602336)
Priority Application: US 95390604 19950217
Designated States: AL AM AT AU AZ BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU IS JP KE KR KZ LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI TM TR TT UA UG US UZ VN KE LS MW SD SZ UG AZ BY KG KZ MD RU TJ TM AT BE DK ES FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN ML MR NE SN
Publication Language: English
Fulltext Word Count: 27047

English Abstract
The present invention describes novel methods of constructing recombinant **adenoviral** vectors capable of expressing human cDNAs, such as wild-type **p53** , WAF1/Cip1/p21, p27/kip1, E. coli cytosine deaminase, wild-type p16, TAM 67 (a jun/fos dominant negative mutant) and B7-1 and B7-2. The invention further provides methods of inhibiting the proliferation of cells, inhibiting the cell cycle of proliferating cells, and methods for the eradication of cells, especially **cancer** and diseased cells, by infecting the cells with a recombinant **adenovirus** vector capable of expressing human cDNAs. Compositions and methods of the invention are suitable for treatment of a subject afflicted with a **tumor** wherein the cells of the **tumor** , for example, lack the wild-type **p53** allele and/or possess a mutated **p53** gene. The invention additionally provides a method for the use of **adenoviral** vectors in the treatment of **cancer** cells, such as lung **cancer** and breast **cancer** cells. The invention further provides methods for the use of **adenoviral** vectors in **cancer** **gene therapy** as a mechanism for purging bone marrow cells of contaminanting **tumor** cells, for eradicating **cancer** cells, and for preventing development of **cancer** cells and tumors.

French Abstract
Cette invention se rapporte a de nouveaux procedes pour construire des vecteurs **adenoviraux** recombines, capables d'exprimer des ADNc humains, tels que **p53** de type sauvage, WAF1/Cip1/p21, p27/kip1, desaminase de cytosine de E. coli, p16 de type sauvage, TAM 67 (un mutant negatif dominant jun/fos) et B7-1 et B7-2. Cette invention se rapporte en outre a des procedes pour inhiber la proliferation de cellules, pour inhiber le cycle de cellules proliferantes, et a des procedes pour eradiquer des cellules, en particulier des cellules cancereuses et malades, en infectant ces cellules avec un vecteur d'**adenovirus** recombine capable d'exprimer des ADNc humains. Des compositions et des procedes objets de cette invention peuvent servir a traiter des sujets souffrant d'une tumeur, dont des cellules sont privees de l'allele **p53** de type sauvage et/ou possedent un gene **p53** ayant subi une mutation. Cette invention se rapporte en outre a un procede d'utilisation de vecteurs **adenoviraux** dans le traitement de cellules cancereuses, telles que des cellules du **cancer** des poumons et des cellules du **cancer** du sein. Cette invention se rapporte en outre a des procedes d'utilisation de vecteurs **adenoviraux** dans la therapie genique du **cancer** , comme mecanisme pour

purger les cellules de la moelle osseuse des cellules tumorales contaminantes, pour eradiquer les cellules cancereuses et pour empecher le developpement de cellules cancereuses et de tumeurs.

27/3,AB/21 (Item 15 from file: 349)
DIALOG(R)File 349:PCT Fulltext

00398276
COMPOSITIONS COMPRISING DNA DAMAGING AGENTS AND P53
COMPOSITIONS COMPRENANT DES AGENTS DE DETERIORATION DE L'ADN ET P53
Patent Applicant/Assignee:
BOARD OF REGENTS THE UNIVERSITY OF TEXAS SYSTEM
Inventor(s):
ROTH Jack A
FUJIWARA Toshiyoshi
GRIMM Elizabeth A
MUKHOPADHYAY Tapas
ZHANG Wei-Wei
OWEN-SCHAUB Laurie B
Patent and Priority Information (Country, Number, Date):
Patent: WO 9528948 A1 19951102
Application: WO 95US4898 19950424 (PCT/WO US9504898)
Priority Application: US 94233002 19940425
Designated States: AM AT AU BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU IS JP KE KG KP LK LR LT LU LV MD MG MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TT UA KE MW SD SZ UG AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE BF BJ CF CM GA GN ML MR NE SN TD TG
Publication Language: English
Fulltext Word Count: 20807

English Abstract
The present invention relates to the use of **tumor** suppressor genes in combination with a DNA damaging agent or factor for use in killing cells, and in particular cancerous cells. A **tumor** suppressor gene, **p53** , was delivered via a recombinant **adenovirus** -mediated gene transfer both in vitro and in vivo, in combination with a chemotherapeutic agent. Treated cells underwent apoptosis with specific DNA fragmentation. Direct injection of the **p53** -**adenovirus** construct into tumors subcutaneously, followed by intraperitoneal administration of a DNA damaging agent, cisplatin, induced massive apoptotic destruction of the tumors. The invention also provides for the clinical application of a regimen combining gene replacement using replication-deficient wild- type **p53** **adenovirus** and DNA-damaging drugs for treatment of human **cancer** .

French Abstract
L'invention concerne l'utilisation de genes suppresseurs de tumeur combines a un agent ou un facteur de deterioration de l'ADN s'utilisant pour detruire des cellules et, en particulier, des cellules cancereuses. On a administre un gene suppresseur de tumeur, **p53** , au moyen d'un transfert de gene induit par un **adenovirus** de recombinaison, a la fois in vitro et in vivo, combine a un agent chimiotherapique. Les cellules traitees ont subi une apoptose avec une fragmentation specifique de l'ADN. L'injection directe du produit genetique **p53** - **adenovirus** dans les tumeurs par voie sous-cutanee, suivie par l'administration intraperitoneale d'un agent de deterioration de l'ADN, la cisplatine, a provoque une destruction massive apoptotique des tumeurs. L'invention concerne egalement la mise en application clinique d'un traitement combinant le remplacement des genes au moyen d'un **adenovirus** de **p53** de type sauvage a replication deficiente et des medicaments de

deterioration de l'ADN, afin de traiter le **cancer** chez l'homme.

27/3,AB/22 (Item 16 from file: 349)
DIALOG(R)File 349:PCT Fulltext

00396149
AN ADENOVIRUS **SUPERVECTOR SYSTEM**
SYSTEME SUPERVECTEUR ADENOVIRAL
Patent Applicant/Assignee:
BOARD OF REGENTS THE UNIVERSITY OF TEXAS SYSTEM
Inventor(s):
ZHANG Wei-Wei
ROTH Jack
Patent and Priority Information (Country, Number, Date):
Patent: WO 9527071 A2-A3 19951012
Application: WO 95US4138 19950404 (PCT/WO US9504138)
Priority Application: US 94222285 19940404
Designated States: AM AT AU BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU IS JP KE KG KP LK LR LT LU LV MD MG MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TT UA VN KE MW SD SZ UG AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE BF BJ CI CM GA GN ML MR NE SN TD TG
Publication Language: English
Fulltext Word Count: 13264

English Abstract
An **adenoviral** supervector system is disclosed that is capable of expressing more than 7.5 kilobases of heterologous DNA in a replication defective **adenoviral** vector. The supervector system comprises an **adenoviral** vector construct and a helper cell. The vector construct is capable of being replicated and packaged into a virion particle in the helper cell. In particular, the helper cell expresses DNA from the E2 region of the **adenovirus** 5 genome and complements deletions in that region in the vector construct. In certain embodiments, the disclosed invention comprises tissue specific expression of up to 30 kb of heterologous DNA directed by an **adenoviral** vector. Also disclosed are methods of transferring heterologous DNA into mammalian cells.

French Abstract
La presente invention concerne un systeme supervecteur **adenoviral** capable d'exprimer au moins 7,5 kilobases d'ADN heterologue dans un vecteur de replication **adenoviral** defectueux. Le systeme supervecteur comporte un vecteur **adenoviral** obtenu par recombinaison et une cellule auxiliaire. Le vecteur obtenu par recombinaison est capable de replication et d'encapsidation dans une particule de virion a l'interieur d'une cellule auxiliaire En l'occurrence, la cellule auxiliaire exprime l'ADN a partir de la region E2 du genome de l'**adenovirus** de type 5 et complete ce qui a ete supprime dans cette region du vecteur obtenu par recombinaison. Dans certains modes de realisation, la presente invention concerne une expressions tissulaire specifique pouvant atteindre 30 kilobases d'ADN heterologue et dirigee par un vecteur **adenoviral** . L'invention concerne egalement des procedes de transfert de l'ADN heterologue vers l'interieur des cellules des mammiferes.
?

28/3,AB/1 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08617214 96134356
Adenoviral - p53 **gene transfer to orthotopic and peritoneal murine bladder** cancer.
Werthman PE; Drazan KE; Rosenthal JT; Khalili R; Shaked A
Department of Surgery, University of California at Los Angeles 90095, USA.
Journal of urology (UNITED STATES) Feb 1996, 155 (2) p753-6, ISSN 0022-5347 Journal Code: KC7
Contract/Grant No.: P01 CA59326, CA, NCI
Languages: ENGLISH
Document type: JOURNAL ARTICLE
PURPOSE: This study was designed to examine the potential for **adenoviral** -mediated **gene therapy** in primary and metastatic bladder **cancer** . MATERIALS AND METHODS: Orthotopic and intraperitoneal bladder tumors were established after delivery of 1 x 10(6) MBT-2 cells into syngeneic mice. Gene transfer was accomplished via intravesical or intraperitoneal instillation by using an **E -1** deleted **adenovirus** encoding LacZ or human **p53** . Successful **tumor** transduction was confirmed in **tumor** DNA and mRNA by polymerase chain reaction. Detection of recombinant gene product was detected by histochemical staining (X-gal) and Western blot. RESULTS: Palpable tumors developed 18 days following implantation. LacZ and **p53** mRNA were present in **tumor** and adjacent normal tissue after bladder and intraperitoneal vector administration. Recombinant gene products were identified by histochemistry and Western blot. CONCLUSION: Bladder **tumor** -directed gene transfer using **adenoviral** vectors is an efficient and powerful tool for evaluating the adjuvant role of therapeutic gene products.

28/3,AB/3 (Item 1 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

05116603 Genuine Article#: VB415 Number of References: 95
Title: ADENOVIRUS **TYPE-5 EARLY REGION-4 IS RESPONSIBLE FOR E1A-INDUCED P53-INDEPENDENT APOPTOSIS** (Abstract Available)
Author(s): MARCELLUS RC; TEODORO JG; WU T; BROUGH DE; KETNER G; SHORE GC; BRANTON PE
Corporate Source: MCGILL UNIV,DEPT BIOCHEM,3655 DRUMMOND ST,MCINTYRE MED SCI BLDG/MONTREAL/PQ H3G 1Y6/CANADA/; MCGILL UNIV,DEPT ONCOL/MONTREAL/PQ H3G 1Y6/CANADA/; GENVEC/ROCKVILLE//MD/20852; JOHNS HOPKINS MED INST,SCH HYG & PUBL HLTH/BALTIMORE//MD/21205
Journal: JOURNAL OF VIROLOGY, 1996, V70, N9 (SEP), P6207-6215
ISSN: 0022-538X
Language: ENGLISH Document Type: ARTICLE
Abstract: In the absence of E1B, the 289- and 243-residue E1A products of human **adenovirus** type 5 induce **p53** -dependent apoptosis. However, our group has shown recently that the 289-residue E1A protein is also able to induce apoptosis by a **p53** -independent mechanism (J. G. Teodoro, G. C. Shore, and P. E. Branton, Oncogene 11:467-473, 1995). Preliminary results suggested that **p53** -independent cell death required expression of one or more additional **adenovirus** early gene products. Here we show that both the E1B 19-kDa protein and cellular Bcl-2 inhibit or significantly delay **p53** -independent apoptosis. Neither early region E2 or E3 appeared to be necessary for such cell death. Analysis of a series of E1A mutants indicated that mutations in

the transactivation domain and other regions of E1A correlated with E1A-mediated transactivation of E4 gene expression. Furthermore, **p53** -deficient human SAOS-2 cells infected with a mutant which expresses E1B but none of the E4 gene products remained viable for considerably longer times than those infected with wild-type **adenovirus** type 5. In addition, an **adenovirus** vector lacking both **E1** and E4 was unable to induce DNA degradation and cell killing in E1A-expressing cell lines. These data showed that an E4 product is essential for E1A-induced **p53** -independent apoptosis.

28/3,AB/4 (Item 2 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

05038990 Genuine Article#: TL083 Number of References: 44
Title: CYTOTOXIC EFFECTS OF ADENOVIRUS-**MEDIATED WILD-TYPE** P53 **PROTEIN EXPRESSION IN NORMAL AND** TUMOR **MAMMARY EPITHELIAL-CELLS** (Abstract Available)
Author(s): KATAYOSE D; GUDAS J; NGUYEN H; SRIVASTAVA S; COWAN KH; SETH P
Corporate Source: NCI,MED BRANCH,MED BREAST CANC SECT,BLDG 10,ROOM 12C210/BETHESDA//MD/20892; NCI,MED BRANCH,MED BREAST CANC SECT/BETHESDA//MD/20892; UNIFORMED SERV UNIV HLTH SCI,DEPT SURG,CTR PROSTATE DIS RES/BETHESDA//MD/20814
Journal: CLINICAL CANCER RESEARCH, 1995, V1, N8 (AUG), P889-897
ISSN: 1078-0432
Language: ENGLISH Document Type: ARTICLE
Abstract: To evaluate the effects of the wild-type **p53** expression in normal and **tumor** cells, we have constructed a recombinant **adenovirus** vector (**E1** minus) expressing human wildtype **p53** cDNA (AdWTp53). Infection of normal and **tumor** cells of lung and mammary epithelial origin with AdWTp53 resulted in high levels of wild type **p53** expression. Production of **p53** protein following infection was dependent on the dose of AdWTp53 with maximum amounts of **p53** produced following infection with 50 plaque-forming units/cell, AdWTp53 infection inhibited the growth of all human cell lines studied, However, **tumor** cells that were null for **p53** prior to infection (H-358 and MDA-MB-157) and **tumor** cells that expressed mutant endogenous **p53** protein (MDA-MB-231 and MDA-MB-453) were more sensitive to AdWTp53 cytotoxicity than cells that contained the wild-type **p53** (MCF-7, MCF-10, 184B5, and normal mammary epithelial cells), All cells exhibited WAF1/Cip1 mRNA and protein induction following AdWTp53 infection. AdWTp53-induced cytotoxicity of human **tumor** cell lines expressing mutant **p53** was mediated by apoptosis as revealed by nucleosomal DNA fragmentation analysis, No detectable nucleosomal DNA fragmentation was observed following AdWTp53 infection of human cells expressing wild-type **p53** . These data suggest that endogenous **p53** status is a determinant of AdWTp53-mediated cell killing of human **tumor** cells.

28/3,AB/11 (Item 1 from file: 315)
DIALOG(R)File 315:ChemEng & Biotec Abs

401737 .CEABA Accession No.: 27-12-026161 DOCUMENT TYPE: Journal
Title: P53 gene therapy **for lung** cancer **shows promise.**
CORPORATE SOURCE: MD Anderson Cancer Center USA
JOURNAL: Biotechnol. Business News, Volume: 6, Issue: 133, Page(s): 8-9
ISSN: 09659595
PUBLICATION DATE: 28 Aug 1996 (960828) LANGUAGE: English

ABSTRACT: Results from a trial in which **gene therapy** was used to treat lung **cancer** suggest the technique could be of real promise in the treatment of specific human cancers. In the trial, a retroviral vector was used to deliver the normal **p53 tumour** suppressor gene into the **tumour** of nine patients with recurrent non-small cell lung **cancer** . The tumours in the patients were associated with mutations in **p53** . Three of the nine showed **tumour** regression, another three showed evidence of the **tumour** stabilizing. Other tumours (in the same patients) that were not treated continued to grow. There were no toxic effects associated with the vector and none of the non-**tumour** tissue analysed showed retroviral sequences. Compared with **adenoviruses** , the transduction of retrovirus into **tumour** cells was not very efficient, and studies are now under way using a replication-defective **E1** -deleted **adenovirus** to deliver **p53** .

28/3,AB/13 (Item 2 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

125078559 CA: 125(7)78559h PATENT
Replication-defective adenovirus gene therapy vectors with expression of the therapeutic gene limited to diseased tissue
INVENTOR(AUTHOR): Hallenbeck, Paul L.; Ramsey, William J.; Chiang, Yawen L.; Hammer, Marlene
LOCATION: USA
ASSIGNEE: Genetic Therapy, Inc.; United States Dept. of Health and Human Services
PATENT: PCT International ; WO 9616676 A1 DATE: 960606
APPLICATION: WO 95US15431 (951128) *US 348960 (941128)
PAGES: 75 pp. CODEN: PIXXD2 LANGUAGE: English CLASS: A61K-048/00A; C12N-015/00B; C12N-005/00B DESIGNATED COUNTRIES: AL; AM; AT; AU; BB; BG; BR; BY; CA; CH; CN; CZ; DE; DK; EE; ES; FI; GB; GE; HU; IS; JP; KE; KG; KP; KR; KZ; LK; LR; LS; LT; LU; LV; MD; MG; MK; MN; MW; MX; NO; NZ; PL; PT; RO; RU; SD; SE; SG; SI; SK DESIGNATED REGIONAL: KE; LS; MW; SD; SZ; UG; AT; BE ; CH; DE; DK; ES; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE; BF; BJ; CF; CG; CI; CM; GA; GN; ML; MR; NE; SN; TD; TG

28/3,AB/29 (Item 15 from file: 349)
DIALOG(R)File 349:PCT Fulltext

00361723
DEFECTIVE RECOMBINANT ADENOVIRUSES **FOR** GENE THERAPY **OF TUMOURS**
ADENOVIRUS **RECOMBINANTS DEFECTIFS POUR LA THERAPIE GENIQUE DES TUMEURS**
Patent Applicant/Assignee:
RHONE-POULENC RORER SA
PERRICAUDET Michel
HADDADA Hedi
MAY Evelyne
Inventor(s):
PERRICAUDET Michel
HADDADA Hedi
MAY Evelyne
Patent and Priority Information (Country, Number, Date):
Patent: WO 9424297 A1 19941027
Application: WO 94FR421 19940415 (PCT/WO FR9400421)
Priority Application: FR 934745 19930422
Designated States: AU CA FI HU JP NO NZ US AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE

Publication Language: French
Fulltext Word Count: 3897
English Abstract
Recombinant **adenoviruses** comprising a heterologous DNA sequence, preparation thereof, and use thereof for the treatment and/or prevention of **cancer** .

French Abstract
La presente invention concerne des **adenovirus** recombinants comportant une sequence d'ADN heterologue, leur preparation, et leur utilisation pour le traitement et/ou la prevention des cancers.
?

57/3,AB/2 (Item 1 from file: 266)
DIALOG(R)File 266:FEDRIP

00290006
IDENTIFYING NO.: 5R29CA69546-04 AGENCY CODE: CRISP
P53--DUAL GROWTH CONTROL AND DNA DAMAGE SENSITIZATION
PRINCIPAL INVESTIGATOR: GJERSET, RUTH A
ADDRESS: SIDNEY KIMMEL CANCER CENTER 10835 ALTMAN ROW SAN DIEGO, CA 92121
PERFORMING ORG.: SIDNEY KIMMEL CANCER CENTER, SAN DIEGO, CALIFORNIA
SPONSORING ORG.: NATIONAL CANCER INSTITUTE
FY : 2000
SUMMARY: The focus of this proposal is the link between P53-mediated apoptosis and DNA damage repair, and the possibility of exploiting these pathways to overcome therapy resistance in glioblastoma. This tumor is characterized by an unusually malignant nature, by frequent P53 mutation (50% overall) and by high resistance to all forms of presently available therapy. We have found that glioblastoma cells expressing endogenous mutant P53 become much more sensitive to cisplatin and radiation-induced apoptosis following gene transfer of wild-type P53, even under conditions where overall growth of the cells is not significantly changed. In light of the potential clinical interest of this observation for glioblastoma, the project will address: (1) the generality of the sensitization effect in vitro with respect to different P53 mutations, including those which act as dominant-negatives, and with respect to different drugs, (2) The role of DNA-mediated suppression. In particular, we will explore a novel approach to therapy sensitization using P53 along with inhibitors of the AP-1 transcription factor which regulates expression of several DNA repair enzymes. The combined effects will be examined of P53 with each of two AP-1 inhibitors, a dominant-negative inhibitor of c-jun (mutant jun) that inhibits the phosphorylation-rated functions a AP-1 associated with cellular transformation, and the synthetic retinoid, **SR11220** , capable of down-regulating AP-1 activity, (3) The specific components of DNA repair that affect P53-mediated suppression, (4) The in vivo application of P53 combination approaches using a subcutaneous nude mouse model and a fisher rat intracranial model of glioblastoma. These studies are designed to provide a rigorous pre-clinical evaluation of P53-mediated growth suppression and therapy sensitization, and to fully explore the combine potential of P53 and ap-1 inhibitors, as potential second generation anti-cancer agents with specificity for tumor cells. The studies will also provide insight into the fundamental nature of drug and radiation resistance in glioblastoma.

57/3,AB/3 (Item 1 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

130104932 CA: 130(9)104932z JOURNAL
ET-1 expression and growth inhibition of prostate cancer cells: a retinoid target with novel specificity
AUTHOR(S): Hsu, Ju-Yu; Pfahl, Magnus
LOCATION: Sidney Kimmel Cancer Center, San Diego, CA, 92121, USA
JOURNAL: Cancer Res. DATE: 1998 VOLUME: 58 NUMBER: 21 PAGES: 4817-4822 CODEN: CNREA8 ISSN: 0008-5472 LANGUAGE: English PUBLISHER: AACR Subscription Office

57/3,AB/5 (Item 2 from file: 349)
DIALOG(R)File 349:PCT Fulltext

00402757

NOVEL COMPOUNDS USEFUL IN MODULATING GENE EXPRESSION OF RETINOID RESPONSIVE GENES AND/OR HAVING ANTI-AP-1 ACTIVITY

NOUVEAUX COMPOSES UTILES POUR MODULER L'EXPRESSION DE GENES SENSIBLES AUX RETINOIDES ET/OU PRESENTANT UNE ACTIVITE ANTI AP-1

Patent Applicant/Assignee:
SRI INTERNATIONAL
LA JOLLA CANCER RESEARCH FOUNDATION
Inventor(s):
PFAHL Magnus
LEE Mi-Ock
DAWSON Marcia I
HOBBS Peter D
FANJUL Andrea
JONG Ling
GRAUPNER Gerhart
LU Xian-Ping
ZHANG Xiao-Kun

Patent and Priority Information (Country, Number, Date):
Patent: WO 9533745 A2-A3 19951214
Application: WO 95US7390 19950607 (PCT/WO US9507390)
Priority Application: US 94255345 19940607; US 94326775 19941020; US 95468035 19950606
Designated States: AM AT AU BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU IS JP KE KG KP LK LR LT LU LV MD MG MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TT UZ VN KE MW SD SZ UG AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE BF CG CI CM GA GN ML MR NE SN TD TG
Publication Language: English
Fulltext Word Count: 31275

English Abstract
Novel compounds are provided which are useful for the regulation of gene expression by retinoids; these compounds are represented by structural formula (I), wherein the substituents R1 through R5 are as defined herein. Additional compounds are provided which are useful for selectively inhibiting AP-1 or an AP-1 component; one group of such compounds is exemplified by structural formula (II), wherein the substituents R1, R2, R20, R21, R22 and R23 are defined herein. Pharmaceutical compositions are provided as well, as are methods of using the compounds in a variety of contexts.

French Abstract
L'invention concerne de nouveaux composes utiles pour reguler l'expression de genes par les retinoides; ces composes sont structures selon la formule (I) dans laquelle les substituants R1 a R5 ont la notation mentionnee dans la description. L'invention concerne egalement des composes utiles pour inhiber de facon selective l'AP-1 ou un constituant de l'AP-1; un groupe de ces composes est structure selon la formule (II) dans laquelle les substituants R1, R2, R20, R21, R22 et R23 ont la notation mentionnee dans la description. L'invention concerne enfin des compositions pharmaceutiques ainsi que des procedes d'utilisation de ces composes dans differents contextes.

57/3,AB/6 (Item 1 from file: 654)

03114102

Utility
DOWN-REGULATION OF DNA REPAIR TO ENHANCE SENSITIVITY TO P53-MEDIATED APOPTOSIS
[Induction of apoptosis in cancer cells following treatment with inhibitors of DNA repair in combination with p53.]

PATENT NO.: 6,054,467
ISSUED: April 25, 2000 (20000425)
INVENTOR(s): Gjerset, Ruth A., San Diego, CA (California), US (United States of America)
ASSIGNEE(s): Sidney Kimmel Cancer Center, (A U.S. Company or Corporation), San Diego, CA (California), US (United States of America) [Assignee Code(s): 43611]
APPL. NO.: 8-675,887
FILED: July 05, 1996 (19960705)

FULL TEXT: 2289 lines

ABSTRACT

The present invention details methods for the treatment of cancer. In particular it concerns the induction of apoptosis in cancer cells following treatment with inhibitors of DNA repair in combination with p53. Treatment of glioblastoma and breast tumor cells with inhibitors of DNA repair induced growth suppression that was a result of p53-mediated apoptosis. Thus it appears that inhibitors of DNA repair in combination with p53 is involved in restoration of p53-mediated apoptosis.
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92/3,AB/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07671535 94051767
Dietary restriction reduces the incidence of NMU-induced mammary tumors and alters retinoid **tissue concentrations in rats.**
Chevalier S; Tuchweber B; Bhat PV; Lacroix A
Departement de Nutrition, Universite de Montreal, Quebec, Canada.
Nutrition and cancer (UNITED STATES) 1993, 20 (2) p187-96, ISSN 0163-5581 Journal Code: 094
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Previous studies suggested a relationship between dietary restriction (DR) effects on mammary carcinogenesis and DR effects on liver retinoids. Therefore, in this study, **retinoid** concentrations were measured by high-performance liquid chromatography in the plasma, liver, and peripheral organs of DR rats with chemically induced carcinogenesis. Rats were **injected** with N-methyl-N- **nitrosourea** (MNU) and maintained on graded levels of DR (reduction of 10-40% from energy ingested by control animals with free access to food). Mammary **tumor** incidence and multiplicity induced by MNU were reduced in relation to the degree of DR, with virtual prevention occurring at 30% and 40% DR. Total hepatic **retinoid** concentrations (retinol + retinyl esters) were significantly greater in rats given MNU and subjected to DR, but liver total **retinoid** content was comparable between the groups. However, plasma retinol concentrations were significantly lower in DR rats than in controls given the carcinogen without DR. **Retinoid** concentrations were also elevated in adipose tissue, lungs, and intestine of DR rats, while renal concentrations remained unaltered. **Retinoid** concentrations in mammary glands and mammary tumors were similar in all groups. Thus, in DR rats, vitamin A concentrations in liver and other target tissues are maintained or increased despite decreases in plasma. It remains to be investigated whether these alterations in **retinoid** content have any relationship to the **cancer** -preventive effect of DR.

92/3,AB/3 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06845600 92110788
Effects of 3 - aminobenzamide **on the post-initiation phase of N-nitrosobis(2-oxopropyl)amine induced pancreatic carcinogenesis in Syrian hamsters.**
Tsujiuchi T; Mizumoto K; Tsutsumi M; Denda A; Amanuma T; Kondoh S; Konishi Y
Department of Oncological Pathology, Cancer Center, Nara Medical College, Japan.
Cancer letters (NETHERLANDS) Dec 9 1991, 61 (1) p61-6, ISSN 0304-3835 Journal Code: CMX
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Effects of **3 -aminobenzamide** (ABA) on pancreatic carcinogenesis after initiation by N-nitrosobis(2-oxopropyl)amine (BOP) were investigated in Syrian hamsters. Animals were given BOP at a dose of 70 mg/kg body weight by subcutaneous **injection** and following a 2-week recovery period, were administered basal diet or basal diet containing 0.5, 0.75 and 1.5% ABA for 30 weeks. While the incidences of resultant pancreatic lesions, including hyperplasia, atypical hyperplasia and **carcinoma** , induced by BOP were not

significantly influenced by ABA treatment, the mean numbers of those pancreatic lesions were significantly decreased in a dose-dependent way. The results therefore suggested the possible involvement of poly(ADP-ribosyl)ation in the post-initiation phase of pancreatic carcinogenesis in hamsters.

92/3,AB/4 (Item 4 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06652972 91096162
Effects of alkylating antineoplastics alone or in combination with 3-aminobenzamide **on genotoxicity, antitumor activity, and NAD levels in human lymphocytes in vitro and on Ehrlich ascites** tumor **cells in vivo.**
Petrou C; Mourelatos D; Mioglou E; Dozi-Vassiliades J; Catsoulacos P
Department of Medicinal Biology and Genetics, Faculty of Medicine, Aristotelian University, Thessaloniki.
Teratogenesis, carcinogenesis, and mutagenesis (UNITED STATES) 1990, 10 (4) p321-31, ISSN 0270-3211 Journal Code: VM9
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Enhanced cytogenetic damage by the homo-aza-steroidal ester of p-bis(2-chloroethyl)-aminophenylacetic acid (ASE) was observed when human lymphocytes in vitro or Ehrlich ascites **tumor** (EAT) cells in vivo were exposed to nontoxic concentrations of 3-amino-benzamide (3-AB). 3-AB at these concentrations was found to enhance synergistically the cytogenetic damage induced in vivo by **cyclophosphamide** (CP), a metabolically activated chemotherapeutic, or chlorambucil (CBC) in EAT cells. One hour before i.p. **injection** of 5-bromodeoxyuridine (BrdUrd) adsorbed to activated charcoal, EAT-bearing mice treated i.p. with ASE or CP showed a dose-dependent increase in sister chromatid exchange (SCE) rates and cell division delays. The treatment of human lymphocytes in vitro with ASE led to the depletion of cellular NAD, and addition of 3-AB, a potent inhibitor of poly(ADP-ribose)polymerase [P(ADPR)polymerase], to ASE-treated human lymphocytes prevented the drop of NAD, which remained at approximately control levels. Also, the in vivo treatment of EAT cells with CBC, ASE, or CP led to the depletion of NAD, whereas addition of 3-AB to CBC-, ASE- or CP-treated cells prevented the drop of NAD, which remained at nearly control levels. 3-AB in conjunction with CBC, ASE, or CP increased the survival time of the EAT-bearing mice and markedly reduced the ascitic volume. Thus cytogenetic damage induced by ASE plus 3-AB in vitro and by CBC, ASE, or CP plus 3-AB in vivo correlates well with 1) the prevention of NAD depletion in the presence of 3-AB in cells treated with the same alkylating agents in vitro or in vivo and 2) the in vivo antitumor effect by ASE, CBC, or CP in combination with 3-AB.

92/3,AB/6 (Item 6 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

05975243 86133943
Retinoid-tamoxifen interaction in mammary cancer **chemoprevention.**
McCormick DL; Moon RC
Carcinogenesis (UNITED STATES) Feb 1986, 7 (2) p193-6, ISSN 0143-3334 Journal Code: C9T
Contract/Grant No.: NO1-CP-05718, CP, NCI
Languages: ENGLISH
Document type: JOURNAL ARTICLE
The synthetic **retinoid** , N-(4-hydroxyphenyl)retinamide (4-HPR), and

bilateral ovariectomy act synergistically to inhibit mammary **cancer** induction in female rats. Two parallel studies were conducted to determine if a similar interaction would be obtained with 4-HPR and the anti-estrogen, tamoxifen. Fifty-day-old, virgin, female Sprague-Dawley rats were given a single i.v. **injection** of 50 mg N-methyl-N-**nitrosourea** /kg body weight. Beginning 7 days post-carcinogen, groups of 30 rats were administered 4-HPR (391 or 782 mg/kg diet) and/or tamoxifen (2.5, 5, 10 or 100 micrograms s.c. three times per week); controls received a placebo diet and injections of vehicle only. Exposure to 4-HPR alone or tamoxifen alone reduced mammary **cancer** multiplicity and increased **tumor** latent period compared with the control. Combined administration of 4-HPR plus tamoxifen resulted in an enhanced inhibition of mammary carcinogenesis and caused a significant reduction in **tumor** -related mortality. These data suggest that **retinoid** administration may provide a means to increase the efficacy of hormonal manipulation in **cancer** prevention and therapy.

92/3,AB/13 (Item 1 from file: 73)
DIALOG(R)File 73:EMBASE

04906258 EMBASE No: 1992046473
Multidisciplinary treatment of facial skin cancer
Calhoun K.H.; Wagner R.F.
Department of Otolaryngology, University of Texas Medical Branch, Galveston, TX 77550 United States
Texas Medicine (TEX. MED.) (United States) 1991, 87/12 (64-69)
CODEN: TXMDA ISSN: 0040-4470
DOCUMENT TYPE: Journal; Short Survey
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

Skin **cancer** incidence is increasing rapidly. We outline the indications for and advantages of diagnostic techniques and treatments, including curettage and electrodesiccation, surgical excision, Mohs' micrographic surgery, cryosurgery, **radiation** therapy, interferon **injection** , and photodynamic therapy. We describe our interdisciplinary treatment protocol for skin **cancer** treatment and emphasize avoidance of the sun and early treatment of photodamaged skin. This treatment includes oral retinoids, topical tretinoin (Retin-A), 5 fluorouracil, and chemical peels performed with trichloroacetic acid or phenol.

92/3,AB/15 (Item 1 from file: 266)
DIALOG(R)File 266:FEDRIP

00286309
IDENTIFYING NO.: 3P01CA05826-37S1 0143 AGENCY CODE: CRISP
DEVELOPMENTAL CHEMOTHERAPY
PRINCIPAL INVESTIGATOR: SPRIGGS, DAVID R
ADDRESS: SLOAN-KETTERING INST CANCER RE 1275 YORK AVE NEW YORK, NY 10021
PERFORMING ORG.: SLOAN-KETTERING INSTITUTE FOR **CANCER** RES, NEW YORK, NEW YORK
SPONSORING ORG.: NATIONAL **CANCER** INSTITUTE
FY : 2000
SUMMARY: The objectives listed for project 1 in the last grant submission have been successfully addressed during the most recent funding period. The following major accomplishments may be cited as a consequence of the activities of Project 1: (1) DIFFERENTIATION: Since the last grant submission, MSKCC has been a leading center of the development and rational application of all trans-retinoic acid therapy for the treatment of acute

promyelocytic **leukemia** . Studies supported by this program included studies of the pharmacokinetics and metabolism of all trans retinoic acid, its toxicity and its efficacy in the treatment of acute promyelocytic **leukemia** . (2) DRUG MODULATION AND RESISTANCE: Clinical trials of idarubicin, liposomal **doxorubicin** and intra hepatic verapamil have been completed. Combination studies of Edatrexate and established chemotherapy agents are continuing. (3) NEW AGENT DEVELOPMENT: A variety of new agents have been tested including edatrexate, lometrexol, deoxyspergualin, topotecan and chloroquinoloxalone sulfonamide.

In the next funding period, we will continue our early drug development studies, focused on Phase I and Pharmacology studies of putative differentiation agents, modulation studies and new combination studies. The purpose of project 1 will be to provide Phase I toxicity and pharmacology data on promising new approaches to chemotherapy which can then be applied in a disease specific manner in both projects 2 and 3. The Specific Aims will be 1) To determine the clinical toxicity and pharmacology of PUTATIVE DIFFERENTIATION INDUCING AGENTS, including a new **retinoid** LNG 1069, phenylbutyrate, and a new analog of hexamethylene bisacetamide. 2) To conduct a dose escalation study of lobaplatin, a chemotherapy agent which appears to be good candidate for HIGH DOSE THERAPY with growth factor and autologous stem cell support. 3) To determine the effect of RESISTANCE MODULATING AGENTS on the toxicity and pharmacology of established anticancer agents. The modulating agents to be studied include carboxypeptidase G2, and edatrexate leucovorin. 4) To conduct phase I / pharmacology studies of NEW AGENTS AND COMBINATIONS which appear to be synergistic in preclinical studies. These studies will include Phase I studies of the murine/human chimeric antibody HC225 with CDDP, desoxyspergualin and murine antibody cc49, and edatrexate with CDDP / **taxol** as well as an adaptive control study of 96 h **taxol** /cddp.

92/3,AB/32 (Item 8 from file: 349)
DIALOG(R)File 349:PCT Fulltext

00365231
METHODS OF TREATING AND DETECTING CANCER **USING VIRUSES**
PROCEDE DE TRAITEMENT ET DE DETECTION DU CANCER **A L'AIDE DE VIRUS**
Patent Applicant/Assignee:
LORENCE Robert M
REICHARD Kirk W
Inventor(s):
LORENCE Robert M
REICHARD Kirk W
Patent and Priority Information (Country, Number, Date):
Patent: WO 9425627 A1 19941110
Application: WO 94US4732 19940429 (PCT/WO US9404732)
Priority Application: US 9355519 19930430
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Publication Language: English
Fulltext Word Count: 7543

English Abstract
The invention provides a method of treating **cancer** in a mammal comprising administering to the mammal an effective amount of virus, particularly Newcastle Disease Virus or other Paramyxovirus. The invention also provides a method of treating **cancer** in a mammal comprising administering such viruses to the mammal in combination with

another agent such as a chemotherapeutic compound, immunoadjuvant, cytokine, or immunosuppressive agent. The invention further provides a method of detecting **cancer** cells in a mammal using Paramyxovirus as an imaging agent and as an indicator of **cancer** cell growth in the mammal.

French Abstract

L'invention se rapporte a un procede de traitement du **cancer** chez un mammifere, consistant a administrer a ce dernier une dose efficace d'un virus, en particulier le virus de la maladie de Newcastle ou autre Paramyxovirus. L'invention se rapporte egalement a un procede de traitement du **cancer** chez un mammifere, consistant a administrer a ce dernier de tels virus en combinaison avec un autre agent tel qu'un compose chimiotherapeutique, un immunoadjuvant, une cytokine ou un agent immunosuppresseur. L'invention se rapporte en outre a un procede de detection de cellules cancereuses chez un mammifere, ce procede consistant a utiliser un paramyxovirus comme agent d'imagerie et comme indicateur de la croissance de cellules cancereuses chez le mammifere.

92/3,AB/56 (Item 6 from file: 653)

01206572

Utility

NOVEL RETINOIDS AND THEIR USE IN PREVENTING CARCINOGENESIS

PATENT NO.: 4,310,546
ISSUED: January 12, 1982 (19820112)
INVENTOR(s): Gander, Robert J., Whitehouse, NJ (New Jersey), US (United States of America)
ASSIGNEE(s): Johnson & Johnson, (A U.S. Company or Corporation), New Brunswick, NJ (New Jersey), US (United States of America) [Assignee Code(s): 44160]
APPL. NO.: 5-929,093
FILED: July 31, 1978 (19780731)

FULL TEXT: 309 lines

ABSTRACT

Novel N-(4-acyloxyphenyl)-all-trans-retinamide compounds are useful in preventing epithelial **cancer** in mammals.